

**REMARKS****Status of the Claims**

Claims 1-12, 17-21, 27-30, 37-49, 54-58, 63-67, 91-95, and 100-104, 111, 128-130, 138, 151, 164, and 177 have been canceled by previous amendment without prejudice or disclaimer. Accordingly, claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, and 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 are pending and at issue.

**Obviousness-type Double Patenting and Common Ownership Rejections**

Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, and 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 stand rejected under the judicially created doctrine of obviousness-type double patenting over various claims of U.S. Patent Nos. 6,071,538, 5,714,167, 6,348,207 and 6,221,367. Applicants respectfully disagree with the rejection. Upon the finding of allowable subject matter, applicants will consider filing a terminal disclaimer.

**Rejections Under 35 U.S.C. § 103(a)**

Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, and 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 stand rejected as obvious over Makino, et al. (U.S. Patent No. 4,746,675; hereafter "Makino") in view of Morishita, et al. (U.S. Patent No. 4,873,087; hereafter "Morishita").

Applicants respectfully traverse this rejection and request reconsideration.

"To establish a *prima facie* case of obviousness, ... there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of

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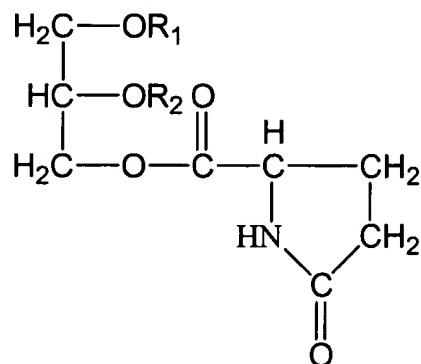
Here, the Examiner has not satisfactorily explained the reasons one of ordinary skill in the art would have been motivated to select and combine Makino and Morishita. The Examiner merely states what each reference teaches, but does not offer any explanation as to why a person would have been motivated to combine the references:

Applicants respectfully submit that the Examiner has not satisfied the Examiner's burden to establish motivation to combine simply based on Makino's purported teaching of a penetration enhancer and oral or injection routes of administration,<sup>1</sup> and Morishita's teaching of compositions

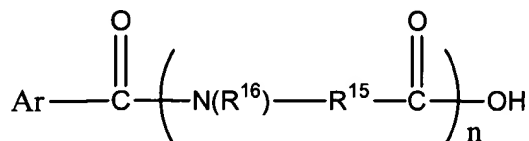
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using different compounds to enhance absorption through the colon, rectum or vagina. In the absence of further reasoning by the Examiner to establish a motivation to combine the references, Applicants submit that the references are not properly combined (Or was Makino properly cited in view of Morishita) and that a *prima facie* case of obviousness has not been established.

Even assuming, *arguendo*, that it was appropriate for the Examiner to combine (or cite Makino in view of Morishita), the references, taken alone or combined, do not teach every limitation of the pending claims and, thus, the obviousness rejection is improper. The claims call for a perturbant selected from either a carboxylic acid or acylated amino acid of specified formulae; neither reference teaches such a perturbant. The Examiner admits that Makino does not teach a carboxylic acid (Office Action of April 19, 2006, at pg. 5, line 11). The Examiner contends, however, that Makino discloses a pyroglutamic acid derivative penetration enhancer that reads on the claimed acylated amino acids. Makino's penetration enhancer has the following formula:



wherein  $R_1$  and  $R_2$  are independently hydrogen,  $C_1$ - $C_{25}$  alkyl,  $C_2$ - $C_{25}$  alkenyl,  $C_1$ - $C_{24}$  alkyl carbonyl or a  $C_2$ - $C_{24}$  alkenyl carbonyl. The presently recited acylated amino acid has the following formula:



Contrary to the Examiner's contention, Makino's penetration enhancer does not read on the claimed acylated amino acid since Makino does not disclose a compound with a terminal COOH group and an uninterrupted, terminal aryl group.

Notwithstanding the Examiner's contention, the accuracy of which need not be argued in this filing, Morishita clearly does not teach or suggest the presently claimed *perturbants* as final products. The compounds disclosed in columns 4 and 6 of Morishita *are merely intermediates* used to produce Morishita's absorption promoter shown in formula I. According to the Manual of Patent Examining Procedure:

(MPEP § 2144.09, *citing, In re Lahu*, 747 F.2d 703 (Fed. Cir. 1994), emphasis added). Therefore, it would not have been obvious to one of ordinary skill in the art to use the *intermediates* of Morishita as perturbants, as claimed.

